AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

What is claimed is:

1. (currently amended) A method for characterising an analyte by matrix assisted laser desorption ionization (MALDI) mass spectrometry, which method comprises:

(a) labelling the analyte with a light-absorbing label that absorbs light at a pre-determined frequency, to form a labelled analyte;

(b) embedding the labelled analyte in a matrix ~~formed from at least one compound that absorbs light~~, wherein the matrix comprises at least one light-absorbing compound, to form an embedded labelled analyte;

(c) desorbing the embedded labelled analyte by exposing it to light having the pre determined frequency, to form a desorbed analyte; and

(d) detecting the desorbed analyte by mass spectrometry, to characterise the analyte.

2. (currently amended) The ~~A~~ method according to claim 1, wherein the desorbed analyte is directly detected by mass spectrometry.

3. (currently amended) The ~~A~~ method according to claim 1, in which the desorbed analyte is indirectly detected by mass spectrometry, wherein the analyte ~~is additionally labelled with~~ further comprises a mass label relatable to the analyte, ~~and wherein the mass label is cleaved~~ which method comprises cleaving the mass label from the desorbed analyte and ~~detected~~ detecting the mass label by mass spectrometry to characterise the analyte.

4. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the light to which the embedded labelled analyte is exposed is laser light.

5. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the ~~compound forming the matrix~~ light-absorbing compound absorbs light at the ~~same frequency as the light-absorbing label~~ pre-determined frequency.

6. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the matrix and light-absorbing label are formed from the same compound.

7. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the matrix is a solid matrix or liquid matrix..

8. (currently amended) The ~~A~~ method according to claim 7, wherein the matrix is a liquid matrix comprising nitrobenzyl alcohol.

9. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the matrix comprises an acid matrix or a basic matrix.

10. (currently amended) The ~~A~~ method according to claim 1 ~~9~~, wherein the matrix comprises ~~a compound selected from~~ 3-hydroxypicolinic acid, 2,5-dihydroxybenzoic acid, or ~~and~~ 4-hydroxy-alpha-cyanocinnamic acid.

11. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the light-absorbing label is formed from a dye.

12. (currently amended) The ~~A~~ method according to claim 11, wherein the dye is a non-fluorescent dye.

13. (currently amended) The ~~A~~ method according to claim ~~11 or~~12, wherein the dye comprises 4-dimethylaminoazobenzine-4'-sulphonyl chloride (dabsyl chloride), 3-hydroxypicolinic acid, 2,5-dihydroxybenzoic acid, or ~~and~~ 4-hydroxy-alpha-cyanocinnamic acid.

14. (currently amended) The ~~A~~ method according to ~~any preceding~~ claim 1, wherein the analyte comprises ~~one or more compounds selected from~~ a protein, a polypeptide, a peptide, a peptide fragment, or ~~and~~ an amino acid.

15. (currently amended) A method for characterising a polypeptide, which method comprises the steps of:

~~(a) optionally reducing cysteine disulphide bridges in the polypeptide to form free thiols, and capping the free thiols;~~

~~(b)~~ (a) cleaving the polypeptide with a sequence specific cleavage reagent to form peptide fragments;

~~(c) optionally deactivating the cleavage reagent;~~

~~(d)~~ (b) capping one or more ε-amino groups that are present with a lysine reactive agent;

~~(e)~~ (c) analyzing the peptide fragments according to the method ~~as defined in any of claims 1-14~~ of claim 1 to form a mass fingerprint for the polypeptide; and

~~(f)~~ (d) determining the identity of the polypeptide from the mass fingerprint.

16. (currently amended) A method for characterising a population of polypeptides, which method comprises the steps of:

~~(h) optionally reducing cysteine disulphide bridges in one or more polypeptides to form free thiols, and capping the free thiols;~~

~~(i)~~ (a) separating one or more polypeptides from the population;

~~(j)~~ (b) cleaving one or more polypeptides with a sequence specific cleavage reagent to form peptide fragments;

~~(k) optionally deactivating the cleavage reagent;~~

~~(l)~~ (c) capping one or more ε-amino groups that are present with a lysine reactive agent;

~~(m)~~ (d) analysing the peptide fragments according to ~~a~~ the method of claim 1 ~~as defined in any of claims 1-14~~ to form a mass fingerprint for one or more polypeptides; and

~~(n)~~ (e) determining the identity of one or more polypeptides from the mass fingerprint.

17. (currently amended) A method for comparing a plurality of samples, each sample comprising one or more polypeptides, which method comprises the steps of:

~~(h) optionally reducing cysteine disulphide bridges in one or more polypeptides to form free thiols, and capping the free thiols;~~

~~(i)~~ (a) separating one or more polypeptides from each of the samples;

~~(j)~~ (b) cleaving the polypeptides with a sequence specific cleavage reagent to form peptide fragments;

~~(k) optionally deactivating the cleavage reagent;~~

~~(l)~~ (c) capping one or more ε-amino groups that are present with a lysine reactive agent;

~~(m)~~ (d) analysing peptide fragments according to ~~a~~ the method of claim 1 ~~as defined in any of claims 1-14~~ to form a mass fingerprint for one or more polypeptides from the samples; and

~~(n)~~ (e) determining the identity of one or more polypeptides in the samples from one or more mass fingerprints.

18. (currently amended) The ~~A~~ method according to ~~any of claims 15-17~~ claim 15, wherein the lysine-reactive agent is a labelled lysine-reactive agent.

19. (currently amended) A method ~~according to claim 17,~~ for comparing a plurality of samples, each sample comprising one or more polypeptides, which method comprises:

~~(a) optionally reducing cysteine disulphide bridges and capping the free thiols in one or more polypeptides from the samples;~~

~~(b)~~ (a) capping one or more ε-amino groups that are present in each sample with a labelled lysine reactive agent;

~~(c)~~ (b) pooling the samples;

~~(d)~~ (c) separating one or more polypeptides from the pooled samples;

~~(e)~~ (d) cleaving the polypeptides with a sequence specific cleavage reagent to form peptide fragments;

~~(f) optionally deactivating the cleavage reagent;~~

~~(g)~~ (e) analyzing peptide fragments according to ~~a~~ the method ~~as defined in any~~ of claim 1 ~~claims 1-14~~ to form a mass fingerprint for one or more polypeptides from the samples; and

~~(h)~~ (f) determining the identity of one or more polypeptides in the samples from one or more mass fingerprints;

wherein the same label is employed for polypeptides or peptides from the same sample, and different labels are employed for polypeptides or peptides from different samples, such that the sample from which a polypeptide or peptide originates can be determined from its label.

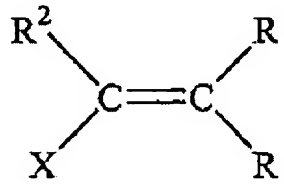
20. (currently amended) The ~~A~~ method according to ~~any of claims 15-19~~ claim 19, wherein the sequence specific cleavage agent cleaves the one or more polypeptides on the C-terminal side of a lysine residue.

21. (currently amended) The ~~A~~ method according to ~~any of claims 15-20~~ claim 19, wherein the specific cleavage agent comprises Lys-C or Trypsin.

22. (currently amended) The ~~A~~ method according to ~~any of claims 15-21~~ claim 19, wherein the peptide fragments having capped ε-amino groups are removed by affinity capture, and wherein the lysine reactive agent comprises biotin.

23. (currently amended) The ~~A~~ method according to ~~any of claims 15-22~~ claim 19, wherein the lysine reactive agent comprises a hindered Michael reagent.

24. (currently amended) The ~~A~~ method according to claim 23, wherein the hindered Michael agent comprises a compound having the following structure:



wherein X is an electron withdrawing group that is capable of stabilizing a negative charge; the R groups independently comprise a hydrogen, a halogen, an alkyl, an aryl, or an aromatic group with the proviso that at least one of the R groups comprises a sterically hindering group; and the group R^2 comprises a hydrogen, a halogen, a hydrocarbon group, an electron withdrawing group, or ~~and/or~~ a linker capable of attachment to an affinity capture functionality or a solid phase support.

25. (original) A labelled analyte compound, which compound has the following structure:

D-M-L-A

wherein D comprises a light absorbing label, M comprises a mass modifier, L comprises a linker and A comprises an analyte.

26. (currently amended) The ~~A~~ compound ~~according to~~ of claim 25, wherein D comprises a non-

fluorescent dye.

27. (currently amended) The ~~A~~ compound ~~according to claim 26~~ of claim 26, wherein ~~D~~ the non-fluorescent dye comprises a cinnamic acid derivative, a nicotinic acid derivative, a picolinic acid derivative, a hydroxybenzoic acid derivative, a methoxybenzoic acid derivative, or a sinapinic acid derivative.

28. (currently amended) The ~~A~~ compound ~~according to claim 26 or claim 27~~ of claim 26, wherein the non-fluorescent dye comprises ~~a compound selected from~~ 4-dimethylaminoazobenzine-4'-sulphonyl chloride (DABSYL chloride), 3-hydroxypicolinic acid, 2,5-dihydroxybenzoic acid ~~and~~, or 4-hydroxy-alpha-cyanocinnamic acid.

29. (currently amended) The ~~A~~ compound ~~according to any of claims 25-28~~ of claim 25, wherein M is ~~selected from~~ a compound formed from an aryl ether[~~,~~] or an oligomer formed from 2 or more aryl ether units.

30. (currently amended) The ~~A~~ compound ~~according to any of claims 25-28~~ of claim 25, wherein the linker comprises ~~a group selected from~~ $-CR_2-CH_2-SO_2-$, $-N(CR_2-CH_2-SO_2-)_2$, $-NH-CR_2-CH_2-SO_2-$, -CO-NH-, -CO-O-, -NH-CO-NH-, -NH-CS-NH-, $-CH_2-NH-$,$-S0_2-NH-$, $-NH-CH_2-CH_2-$ ~~and~~ , or -OP (=O)(O)O-.

31. (currently amended) The ~~A~~ compound ~~according to any of claims 25-30~~ of claim 25, wherein A ~~is selected from~~ comprises a protein, a polypeptide, a peptide, a peptide fragment, or ~~and~~ an amino acid.

32. (currently amended) A compound for labelling an analyte, which compound has the following structure:

~~M-L-R~~ K-L-R

wherein ~~M~~ K is a mass marker comprising a cinnamic acid derivative, a nicotinic acid derivative, a picolinic acid derivative, a hydroxybenzoic acid derivative, a methoxybenzoic acid derivative, or a sinapinic acid derivative; ~~[,]~~ L comprises a linker; and R comprises a reactive functionality for attaching the compound to an analyte.

33. (currently amended) The ~~A~~ compound ~~according to~~ of claim 32 , wherein ~~M~~ K comprises a non-fluorescent dye compound. ~~selected from 4-dimethylaminoazobenzine-4'-sulphonyl chloride (DABSYL chloride), 3-hydroxypicolinic acid, 2,5-dihydroxybenzoic acid, and 4-hydroxy-alpha-cyanocinnamic acid.~~

34. (currently amended) The ~~A~~ compound ~~according to claim 32 or claim 33~~ of claim 32, wherein ~~M~~ K further comprises a compound formed from an aryl ether ~~[,]~~ or an oligomer formed from 2 or more aryl ether units.

35. (currently amended) The ~~A~~ compound ~~according to any of claims 32-34~~ of claim 32, wherein the linker comprises ~~a group selected from~~ $-CR_2-CH_2-SO_2-$, $-N(CR_2-CH_2-SO_2-)_2$, $-NH-CR_2-CH_2-SO_2-$, -CO-NH-, -CO-O-, -NH-CO-NH-, -NH-CS-NH-, $-CH_2-NH-$, $-SO_2-NH-$, $-NH-CH_2-CH_2-$, -OP(=O)(O)O- ~~and~~ , or an amide linkage through the acid groups of M.

36. (currently amended) The ~~A~~ compound ~~according to any of claims 32-35~~ of claim 32, wherein ~~R is for attaching the compound to a protein, a polypeptide, a peptide, a peptide fragment or an amino acid.~~ the analyte is a protein, polypeptide, peptide, peptide fragment, or amino acid.

37. (currently amended) The ~~A~~ compound ~~according to any of claims 32-36,~~ of claim 32, wherein R comprises an ester group, an acid anhydride group, an acid halide group ~~such as an acid chloride,~~ an N-hydroxysuccinamide group, a pentafluorophenyl ester group, a maleimide group, an alkenyl sulphone group, or an iodoacetamide group.

38. (currently amended) The ~~A~~ compound ~~according to any of claims 25-37~~ of claim 25, ~~which compound~~ further ~~comprises~~ comprising an affinity ligand.

39. (currently amended) The ~~A~~ compound ~~according to~~ of claim 38, wherein the affinity ligand comprises biotin.

40. (currently amended) The ~~A~~ compound ~~according to any of claims 25-39~~ of claim 25, ~~which compound~~ further ~~comprises~~ comprising an ionizable moiety.

41. (currently amended) The ~~A~~ compound ~~according to~~ of claim 40, wherein the ionizable moiety is selected from the group consisting of a tertiary amino group, guanidino group, and sulphonic acid group.

42. (currently amended) The ~~A~~ compound ~~according to any of claims 25-41~~ of claim 25, ~~which compound comprises~~ comprising a cinnamic acid functionality.

43. (currently amended) An array ~~of two or more compounds~~ for labelling an analyte, which array comprises two or more compounds of claim 32, wherein each compound has a different mass. ~~wherein the compounds in the array are compounds as defined in any of claims 32-42 and wherein each compound in the array differs in mass from all other compounds in the array.~~

44. (currently amended) ~~An~~ The array of ~~compounds according to~~ claim 43, wherein the difference in mass of each ~~of the compounds in the array~~ compound is achieved by isotopic substitution.

45. (original) A kit for characterising an analyte by matrix assisted laser desorption ionization (MALDI) mass spectrometry, which kit comprises:

(a) one or more light absorbing labels having a reactive functionality for attaching the

label to an analyte; and

(b) a compound for forming a matrix, which compound absorbs light at the same frequency as the light-absorbing label.

46. (currently amended) The ~~A~~ kit ~~according to~~ of claim 45, wherein the ~~component (a)~~ light absorbing label comprises a compound~~, or an array of compounds, as defined in claims 32-44.~~ having the following structure:

~~M-L-R~~ K-L-R

wherein K is a mass marker comprising a cinnamic acid derivative, a nicotinic acid derivative, a picolinic acid derivative, a hydroxybenzoic acid derivative, a methoxybenzoic acid derivative, or a sinapinic acid derivative; L comprises a linker; and R comprises a reactive functionality for attaching the compound to an analyte.

47. (currently amended) A kit for characterising an analyte by matrix assisted laser desorption ionization (MALDI) mass spectrometry, which kit comprises:

(a) ~~a compound, or an array of compounds, as defined in any of claims 32-44;~~ the compound of claim 32; and

(b) an ion exchange resin.

48. (currently amended) The ~~A~~ kit ~~according to~~ of claim 47, wherein the compound ~~or array of compounds~~ comprises an ionizable moiety that forms a positive charge, and wherein the ion exchange resin comprises a cation exchange ~~resin~~.

49. (currently amended) The ~~A~~ kit ~~according to~~ of claim 47, wherein the compound ~~or array of compounds~~ comprises an ionizable moiety that forms a negative charge, and wherein the ion exchange resin comprises an anion exchange ~~resin~~.

50. (new) The method according to claim 3, wherein the mass label is the light-absorbing label.

51. (new) The method according to claim 15, further comprising reducing cysteine disulphide bridges in the polypeptide to form free thiols and capping the free thiols, prior to cleaving the polypeptide.

52. (new) The method according to claim 15, further comprising deactivating the cleavage agent after cleaving the polypeptide.

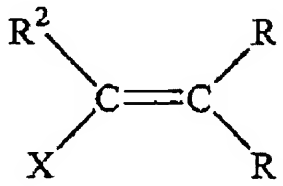
53. (new) The method according to claim 15, wherein the sequence specific cleavage agent cleaves each isolated polypeptide on the C-terminal side of a lysine residue.

54. (new) The method according to claim 15, wherein the sequence specific cleavage agent comprises Lys-C or Trypsin.

55. (new) The method according to claim 15, wherein the peptide fragments having capped ε-amino groups are removed by affinity capture, and wherein the lysine reactive agent comprises biotin.

56. (new) The method according to claim 15, wherein the lysine reactive agent comprises a hindered Michael reagent.

57. (new) The method according to claim 56, wherein the hindered Michael agent comprises a compound having the following structure:



wherein X is an electron withdrawing group that is capable of stabilizing a negative charge; the r groups independently comprise a hydrogen, a halogen, an alkyl, an aryl, or an aromatic group with the proviso that at least one of the R groups comprises a sterically hindering group; and the group R^2 comprises a hydrogen, a halogen, a hydrocarbon group, an electron withdrawing group, or a linker capable of attachment to an affinity capture functionality or a solid phase support.

58. (new) The method according to claim 16, further comprising reducing cysteine disulphide bridges in the polypeptide to form free thiols and capping the free thiols, prior to cleaving the polypeptide.

59. (new) The method according to claim 16, further comprising deactivating the cleavage agent after cleaving the polypeptide.

60. (new) The method according to claim 17, further comprising reducing cysteine disulphide bridges in the polypeptide to form free thiols and capping the free thiols, prior to cleaving the polypeptide.

61. (new) The method according to claim 17, further comprising deactivating the cleavage agent after cleaving the polypeptide.

62. (new) The method according to claim 19, further comprising reducing cysteine disulphide bridges in the polypeptide to form free thiols and capping the free thiols, prior to capping one or more ε-amino groups. .

63. (new) The method according to claim 19, further comprising deactivating the cleavage agent after cleaving the polypeptides.

64. (new) The compound of claim 25, further comprising an affinity ligand.

65. (new) The compound of claim 64, wherein the affinity ligand comprises biotin.

66. (new) The compound of claim 25, further comprising an ionizable moiety.

67. (new) The compound of claim 66, wherein the ionizable moiety is selected from the group consisting of a tertiary amino group, guanidino group, and sulphonic acid group.

68. (new) The compound of claim 25, further comprising a cinnamic acid functionality.

69. (new) The compound of claim 33, wherein the the non-fluorescent dye comprises 4-dimethylaminoazobenzine-4'-sulphonyl chloride (DABSYL chloride), 3-hydroxypicolinic acid, 2,5-dihydroxybenzoic acid, or 4-hydroxy-alpha-cyanocinnamic acid.

70. (new) The compound of claim 37, wherein the acid halide group is acid chloride.